IRF8-dependent DCs play a key role in the regulation of CD8 T cell responses to epithelialderived antigen in the steady state but not in inflammation

Joeris, Thorsten; Gomez-Casado, C.; Holmkvist, P.; Luda, K.; Tavernier, S.; Lambrecht, B. N.; Agace, William Winston

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suppressed Rac activation in neutrophils and consequently inhibited their infiltration to the skin. Unlike 17,18-EpETE, its metabolite 17,18-diHETE did not show any effects on contact hypersensitivity. It was also shown that therapeutic treatment of 17,18-EpETE ameliorated contact hypersensitivity in cynomolgus monkey. These results indicate that 17,18-EpETE could be applied to be a therapeutic agent for the control of allergic inflammatory diseases.

Dendritic Cells 2

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IRF8-dependent DCs play a key role in the regulation of CD8 T cell responses to epithelial-derived antigen in the steady state but not in inflammation

Joeris, T.[1,2], Gomez Casado, C.[2], Holmkvist, P.[2], Luda, K.[2], Tavernier, S.[3], Lambrecht, B.N.[3], Agace, W.W.[1,2]
[1]Danish Technical University - DTU, National Veterinary Institute - Section of Immunology and Vaccinology, Fredrigsberg C, Denmark, [2]Lund University, Experimental Medical Sciences- Section for Immunology, Lund, Sweden, [3]Inflammation Research Center (IRC), VIB-UGent, Ghent, Belgium

Along the process of epithelial self-renewal, antigens derived from apoptotic intestinal epithelial cells (IECs) are taken up by antigen presenting cells (APCs), transported to the gut-draining lymph nodes and cross-presented to CD8 T cells. In steady state, rapid tolerization of CD8 T cells reactive towards epithelial-derived antigens is crucial to maintain tissue homeostasis. In contrast, infection of IECs by intracellular pathogens requires induction of cytotoxic CD8 T cells (CTLs) towards epithelial-associated, pathogen-derived antigens. Currently, little is known about the regulation of CD8 T cells by intestinal APCs in these two different contexts. Since IRF8-dependent dendritic dells (IRF8-DCs) have superior cross-presenting capabilities, we aimed to investigate their role in this process. IFABP-tOva mice, expressing the model-antigen Ovalbumin (Ova) in IECs, were used as recipients to set up chimeras using either CD11c-cre.Irf8$^{fl/fl}$ bone marrow, which cannot generate IRF8-DCs, or cre-negative Irf8$^{fl/fl}$ control bone marrow. Whereas transfer of Ova-specific CD8 T cells (OT-I cells) to steady state control chimeras resulted in their rapid tolerization, OT-I cells transferred to CD11c-cre.Irf8$^{fl/fl}$ chimeras spontaneously developed into CTLs, causing epithelial destruction and intestinal inflammation. However, when the TLR7-ligand R848 was applied as an inflammatory trigger mimicking viral infection in addition to OT-I transfer, expansion of CTLs occurred at similar rates in both, CD11c-cre.Irf8$^{fl/fl}$ and control chimeras. Taken together, this demonstrates that IRF8-DCs are crucial for the rapid tolerization of CD8 T cells reactive towards epithelial-derived antigen in steady state, but are not essential for the induction of CTLs in an inflammatory setting such as found in infection.

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tRNAs: new regularors of immunity?

Arguello, R.J.[1], Reverendo, M.[1], Terawaki, S.[1], Combes, A.[1], Vu-Manh, T.P.[1], Santos, M.[2], Gatti, E.[1], Pierre, P.[1,2]
[1]CIML, Marseille, France, [2]University of Aveiro, Aveiro, Portugal

Dendritic cells (DCs) respond to microbial cues by activating several coordinated metabolic and gene expression programs that altogether maximize their capacity to orchestrate immune responses. Translation of costimulatory molecules, cytokines and other induced mRNAs is an essential part of the program and it is tightly regulated. Recently, a connection between ribosomal speed of elongation, mRNA stability and protein expression has been found tumors and model organisms. Analysing microarray data, we found that genes involved in tRNAs metabolism were coordinately regulated during the first hours after DC activation, suggesting a role connecting transcriptional and translational programs during DCs maturation. To test this hypothesis, we performed tRNA microarrays, codon usage analysis in DC transcriptomic data, and studied the effect of modulating tRNA metabolic pathways in the capacity of DCs mature in response to different stimuli. We have found, an essential inducible regulatory program in DCs that involves qualitative and quantitative changes in the tRNA

